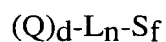
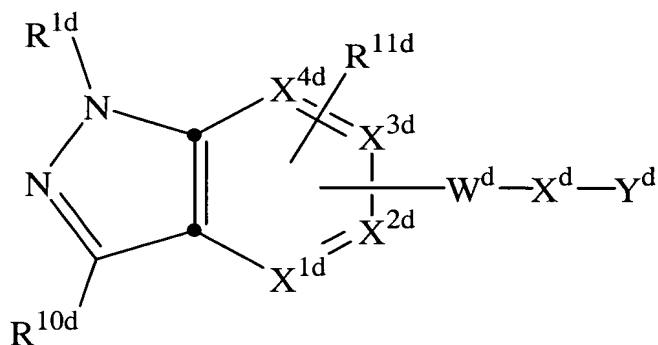


47. (amended) An ultrasound contrast agent composition, comprising:

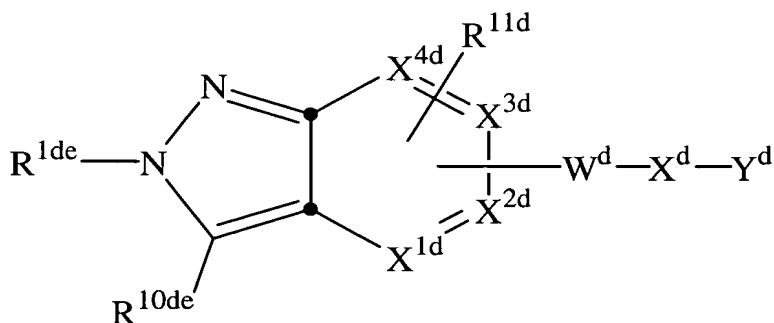
- (a) a compound comprising: an indazole that binds to the integrin $\alpha_v\beta_3$ or $\alpha_v\beta_5$,
a surfactant and a linking group between the indazole and the surfactant;
(b) a parenterally acceptable carrier; and,
(c) an echogenic gas,
wherein said compound is of the formula:



wherein Q is independently a compound of Formulae (Ia) or (Ib):



(Ia)



(Ib)

Cancelled

including stereoisomeric forms thereof, or mixtures of stereoisomeric forms thereof, or pharmaceutically acceptable salt or prodrug forms thereof wherein:

X^{1d} is N, CH, C- W^d - X^d - Y^d , or C- L_n ;

X^{2d} is N, CH, or C- W^d - X^d - Y^d ;

X^{3d} is N, CR^{11d} , or C- W^d - X^d - Y^d ;

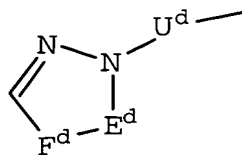
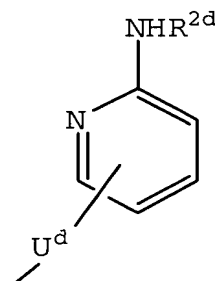
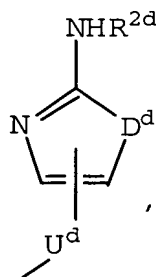
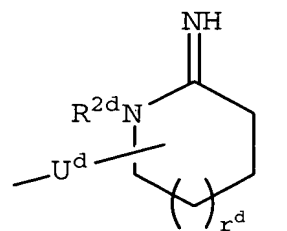
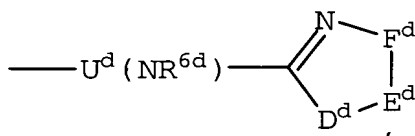
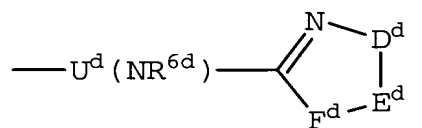
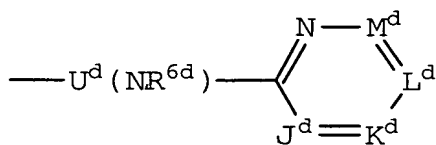
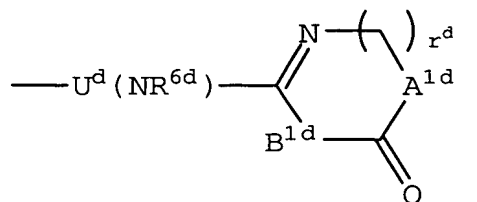
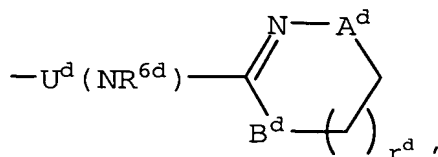
X^{4d} is N or CR^{11d} ;

R^{1d} is selected from: R^{1de} , C_1 - C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_4 - C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} , and aryl(C_1 - C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} ;

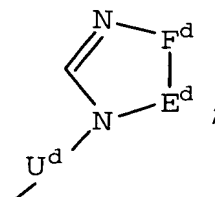
Cancelled

R^{1de} is selected from:

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or



A^d and B^d are independently $-CH_2-$, $-O-$, $-N(R^{2d})-$, or $-C(=O)-$;

A^{1d} and B^{1d} are independently $-CH_2-$ or $-N(R^{3d})-$;

D^d is $-N(R^{2d})-$, $-O-$, $-S-$, $-C(=O)-$ or $-SO_2-$;

E^d - F^d is $-C(R^{4d})=C(R^{5d})-$, $-N=C(R^{4d})-$, $-C(R^{4d})=N-$, or $-C(R^{4d})_2C(R^{5d})_2-$;

J^d , K^d , L^d and M^d are independently selected from:

$-C(R^{4d})-$, $-C(R^{5d})-$ and $-N-$, provided that at least one of J^d , K^d , L^d and M^d is not $-N-$;

provided that when R^{1d} is R^{1de} then one of X^{1d} and X^{2d} is $C-$ W^d - X^d - Y^d , and when R^{10d} is R^{1de} then X^{3d} is $C-$ W^d - X^d - Y^d ;

R^{2d} is selected from: H, C_1 - C_6 alkyl, $(C_1$ - C_6 alkyl)carbonyl, $(C_1$ - C_6 alkoxy)carbonyl; $(C_1$ - C_6 alkyl)aminocarbonyl, C_3 - C_6 alkenyl, C_3 - C_7 cycloalkyl, C_4 - C_{11} cycloalkylalkyl, aryl, heteroaryl(C_1 - C_6 alkyl)carbonyl, heteroarylcarbonyl, aryl(C_1 - C_6 alkyl)-, $(C_1$ - C_6 alkyl)carbonyl-, arylcarbonyl, C_1 - C_6 alkylsulfonyl, arylsulfonyl, aryl(C_1 - C_6 alkyl)sulfonyl, heteroarylsulfonyl, heteroaryl(C_1 - C_6 alkyl)sulfonyl, aryloxy carbonyl, and aryl(C_1 - C_6 alkoxy)carbonyl, wherein said aryl groups are substituted with 0-2 substituents selected from the group consisting of C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo, CF_3 , and nitro;

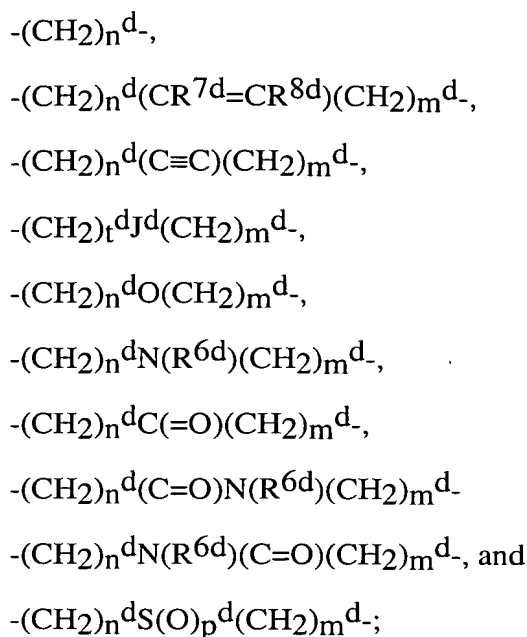
R^{3d} is selected from: H, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_4 - C_{11} cycloalkylalkyl, aryl, aryl(C_1 - C_6 alkyl)-, and heteroaryl(C_1 - C_6 alkyl)-;

R^{4d} and R^{5d} are independently selected from: H, C_1 - C_4 alkoxy, $NR^{2d}R^{3d}$, halogen, NO_2 , CN, CF_3 , C_1 - C_6 alkyl, C_3 - C_6 alkenyl, C_3 - C_7 cycloalkyl, C_4 - C_{11} cycloalkylalkyl, aryl, aryl(C_1 - C_6 alkyl)-, $(C_1$ - C_6 alkyl)carbonyl, $(C_1$ - C_6 alkoxy)carbonyl, arylcarbonyl, or

alternatively, when substituents on adjacent atoms, R^{4d} and R^{5d} can be taken together with the carbon atoms to which they are attached to form a 5-7 membered carbocyclic or 5-7 membered heterocyclic aromatic or non-aromatic ring system, said carbocyclic or heterocyclic ring being optionally substituted with 0-2 groups selected from: C_1 - C_4 alkyl, C_1 - C_4 alkoxy, halo, cyano, amino, CF_3 , and NO_2 ;

Cancelled

U^d is selected from:



wherein one or more of the methylene groups in U^d is optionally substituted with R^{7d} ;

J^d is selected from 1,2-cycloalkylene, 1,2-phenylene, 1,3-phenylene, 1,4-phenylene, 2,3-pyridinylene, 3,4-pyridinylene, 2,4-pyridinylene, and 3,4-pyridazinylene;

R^{6d} is selected from: H, C_1 - C_4 alkyl, or benzyl;

R^{7d} and R^{8d} are independently selected from: H, C_1 - C_6 alkyl, C_3 - C_7 cycloalkyl, C_4 - C_{11} cycloalkylalkyl, aryl, aryl(C_1 - C_6 alkyl)-, and heteroaryl(C_0 - C_6 alkyl)-;

R^{10d} is selected from: H, R^{1de} , C_1 - C_4 alkoxy substituted with 0-1 R^{21d} , $N(R^{6d})_2$, halogen, NO_2 , CN , CF_3 , CO_2R^{17d} , $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, $-SO_2R^{17d}$, $-SO_2NR^{17d}R^{20d}$, C_1 - C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_4 - C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1

R^{21d} , aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} , and aryl(C_1 - C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} ;

R^{10de} is selected from: H, C_1 - C_4 alkoxy substituted with 0-1 R^{21d} , $N(R^{6d})_2$, halogen, NO_2 , CN, CF_3 , CO_2R^{17d} , $C(=O)R^{17d}$, $CONR^{17d}R^{20d}$, $-SO_2R^{17d}$, $-SO_2NR^{17d}R^{20d}$, C_1 - C_6 alkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_6 alkenyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_3 - C_7 cycloalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , C_4 - C_{11} cycloalkylalkyl substituted with 0-1 R^{15d} or 0-1 R^{21d} , aryl substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} , and aryl(C_1 - C_6 alkyl)- substituted with 0-1 R^{15d} or 0-2 R^{11d} or 0-1 R^{21d} ;

R^{11d} is selected from H, halogen, CF_3 , CN, NO_2 , hydroxy, $NR^{2d}R^{3d}$, C_1 - C_4 alkyl substituted with 0-1 R^{21d} , C_1 - C_4 alkoxy substituted with 0-1 R^{21d} , aryl substituted with 0-1 R^{21d} , aryl(C_1 - C_6 alkyl)- substituted with 0-1 R^{21d} , (C_1 - C_4 alkoxy)carbonyl substituted with 0-1 R^{21d} , (C_1 - C_4 alkyl)carbonyl substituted with 0-1 R^{21d} , C_1 - C_4 alkylsulfonyl substituted with 0-1 R^{21d} , and C_1 - C_4 alkylaminosulfonyl substituted with 0-1 R^{21d} ;

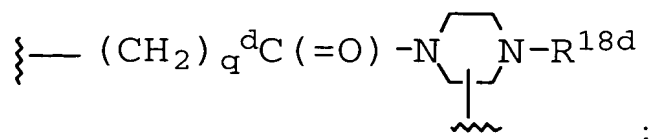
W^d is selected from:

$-(C(R^{12d})_2)_qC(=O)N(R^{13d})-$, and

$-C(=O)-N(R^{13d})-(C(R^{12d})_2)_q-$;

X^d is $-C(R^{12d})(R^{14d})-C(R^{12d})(R^{15d})-$; or

alternatively, W^d and X^d can be taken together to be



R^{12d} is selected from H, halogen, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₇ cycloalkyl, C₄-C₁₀ cycloalkylalkyl, (C₁-C₄ alkyl)carbonyl, aryl, and aryl(C₁-C₆ alkyl)-;

R^{13d} is selected from H, C₁-C₆ alkyl, C₃-C₇ cycloalkylmethyl, and aryl(C₁-C₆ alkyl)-;

R^{14d} is selected from:

H, C₁-C₆ alkylthio(C₁-C₆ alkyl)-, aryl(C₁-C₁₀ alkylthioalkyl)-, aryl(C₁-C₁₀ alkoxyalkyl)-, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxyalkyl, C₁-C₆ hydroxyalkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, C₃-C₁₀ cycloalkylalkyl, aryl(C₁-C₆ alkyl)-, heteroaryl(C₁-C₆ alkyl)-, aryl, heteroaryl, CO₂R^{17d}, C(=O)R^{17d}, and CONR^{17d}R^{20d}, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 0-1 R^{16d} or 0-2 R^{11d};

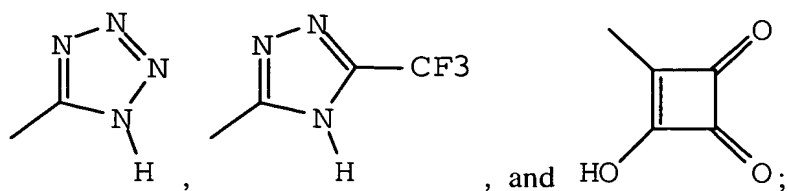
R^{15d} is selected from:

H, R^{16d}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxyalkyl, C₁-C₁₀ alkylaminoalkyl, di(C₁-C₁₀ alkyl)aminoalkyl, (C₁-C₁₀ alkyl)carbonyl, aryl(C₁-C₆ alkyl)carbonyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₁₀ cycloalkyl, C₃-C₁₀ cycloalkylalkyl, aryl(C₁-C₆ alkyl)-, heteroaryl(C₁-C₆ alkyl)-, aryl, heteroaryl, CO₂R^{17d}, C(=O)R^{17d}, CONR^{17d}R^{20d}, SO₂R^{17d}, and SO₂NR^{17d}R^{20d}, provided that any of the above alkyl, cycloalkyl, aryl or heteroaryl groups may be unsubstituted or substituted independently with 0-2 R^{11d};

Y^d is selected from:

-COR^{19d}, -SO₃H, -PO₃H, tetrazolyl, -CONHNHSO₂CF₃, -CONHSO₂R^{17d}, -CONHSO₂NHR^{17d}, -NHCOCF₃, -NHCONHSO₂R^{17d}, -NHSO₂R^{17d}, -OPO₃H₂, -OSO₃H, -PO₃H₂, -SO₃H, -SO₂NHCOR^{17d}, -SO₂NHCO₂R^{17d},

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R^{16d} is selected from:

- N(R^{20d})-C(=O)-O-R^{17d},
- N(R^{20d})-C(=O)-R^{17d},
- N(R^{20d})-C(=O)-NH-R^{17d},
- N(R^{20d})SO₂-R^{17d}, and
- N(R^{20d})SO₂-NR^{20d}R^{17d};

R^{17d} is selected from:

C₁-C₁₀ alkyl optionally substituted with a bond to L_n, C₃-C₁₁ cycloalkyl optionally substituted with a bond to L_n, aryl(C₁-C₆ alkyl)- optionally substituted with a bond to L_n, (C₁-C₆ alkyl)aryl optionally substituted with a bond to L_n, heteroaryl(C₁-C₆ alkyl)- optionally substituted with a bond to L_n, (C₁-C₆ alkyl)heteroaryl optionally substituted with a bond to L_n, biaryl(C₁-C₆ alkyl)- optionally substituted with a bond to L_n, heteroaryl optionally substituted with a bond to L_n, aryl optionally substituted with a bond to L_n, biaryl optionally substituted with a bond to L_n, and a bond to L_n, wherein said aryl, biaryl or heteroaryl groups are also optionally substituted with 0-3 substituents selected from the group: C₁-C₄ alkyl, C₁-C₄ alkoxy, aryl, heteroaryl, halo, cyano, amino, CF₃, and NO₂;

R^{18d} is selected from:

- H,
- C(=O)-O-R^{17d},
- C(=O)-R^{17d},
- C(=O)-NH-R^{17d},
- SO₂-R^{17d}, and

-SO₂-NR^{20d}R^{17d};

R^{19d} is selected from: hydroxy, C₁-C₁₀ alkyloxy, C₃-C₁₁cycloalkyloxy, aryloxy, aryl(C₁-C₆ alkoxy)-, C₃-C₁₀ alkylcarbonyloxyalkyloxy, C₃-C₁₀ alkoxy carbonyloxyalkyloxy, C₂-C₁₀ alkoxy carbonylalkyloxy, C₅-C₁₀ cycloalkylcarbonyloxyalkyloxy, C₅-C₁₀ cycloalkoxy carbonyloxyalkyloxy, C₅-C₁₀ cycloalkoxy carbonylalkyloxy, C₇-C₁₁ aryloxy carbonylalkyloxy, C₈-C₁₂ aryloxy carbonyloxyalkyloxy, C₈-C₁₂ arylcarbonyloxyalkyloxy, C₅-C₁₀ alkoxyalkylcarbonyloxyalkyloxy, C₅-C₁₀ (5-alkyl-1,3-dioxo-cyclopenten-2-one-yl)methyloxy, C₁₀-C₁₄ (5-aryl-1,3-dioxo-cyclopenten-2-one-yl)methyloxy, and

(R^{11d})(R^{12d})N-(C₁-C₁₀ alkoxy)-;

R^{20d} is selected from: H, C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₄-C₁₁ cycloalkylalkyl, aryl, aryl(C₁-C₆ alkyl)-, and heteroaryl(C₁-C₆ alkyl)-;

R^{21d} is selected from: COOH and NR^{6d}₂;

m^d is 0-4;

n^d is 0-4;

t^d is 0-4;

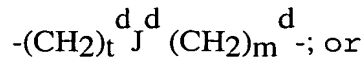
p^d is 0-2;

q^d is 0-2; and

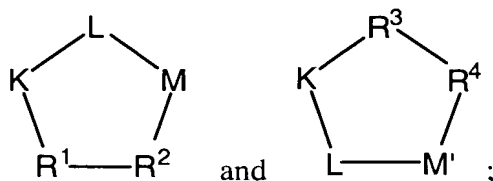
r^d is 0-2;

with the following provisos:

- (1) t^d, n^d, m^d and q^d are chosen such that the number of atoms connecting R^{1d} and Y^d is in the range of 10-14; and
- (2) n^d and m^d are chosen such that the value of n^d plus m^d is greater than one unless U^d is



Q is a peptide selected from the group:



R^1 is L-valine, D-valine or L-lysine optionally substituted on the ϵ amino group with a bond to L_n ;

R^2 is L-phenylalanine, D-phenylalanine, D-1-naphthylalanine, 2-aminothiazole-4-acetic acid or tyrosine, the tyrosine optionally substituted on the hydroxy group with a bond to L_n ;

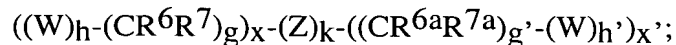
R^3 is D-valine;

R^4 is D-tyrosine substituted on the hydroxy group with a bond to L_n ;

provided that one of R^1 and R^2 in each Q is substituted with a bond to L_n , and further provided that when R^2 is 2-aminothiazole-4-acetic acid, K is N-methylarginine;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

L_n is a linking group having the formula:



W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^8C(=O)$, $C(=O)NR^8$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2 , SO_2NH , $(OCH_2CH_2)_{20-200}$, $(CH_2CH_2O)_{20-200}$, $(OCH_2CH_2CH_2)_{20-200}$, $(CH_2CH_2CH_2O)_{20-200}$, and $(aa)_t$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{10} , C_{3-10} cycloalkyl substituted with 0-3 R^{10} , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{10} ;

R^6 , R^{6a} , R^7 , R^{7a} , and R^8 are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C₁-C₅ alkyl substituted with 0-3 R^{10} , aryl substituted with 0-3 R^{10} , benzyl substituted with 0-3 R^{10} , and C₁-C₅ alkoxy substituted with 0-3 R^{10} , NHC(=O) R^{11} , C(=O)NHR¹¹, NHC(=O)NHR¹¹, NHR¹¹, R^{11} , and a bond to Sf;

R^{10} is independently selected at each occurrence from the group: a bond to Sf, COOR¹¹, C(=O)NHR¹¹, NHC(=O) R^{11} , OH, NHR¹¹, SO₃H, PO₃H, -OPO₃H₂, -OSO₃H, aryl substituted with 0-3 R^{11} , C₁-5 alkyl substituted with 0-1 R^{12} , C₁-5 alkoxy substituted with 0-1 R^{12} , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{11} ;

R^{11} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{12} , aryl substituted with 0-1 R^{12} , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{12} , C₃-10 cycloalkyl substituted with 0-1 R^{12} , and a bond to Sf;

R^{12} is a bond to Sf;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5;

x' is selected from 0, 1, 2, 3, 4, and 5;

Sf is a surfactant which is a lipid or a compound of the

formula: $A^g-E^1-A^{10}$;

A⁹ is selected from the group: OH and OR²⁷;

A¹⁰ is OR²⁷;

R²⁷ is C(=O)C₁₋₂₀ alkyl;

E¹ is C₁₋₁₀ alkylene substituted with 1-3 R²⁸;

R²⁸ is independently selected at each occurrence from the group: R³⁰, -PO₃H-R³⁰, =O, -CO₂R²⁹, -C(=O)R²⁹, -C(=O)N(R²⁹)₂, -CH₂OR²⁹, -OR²⁹, -N(R²⁹)₂, C₁-C₅ alkyl, and C₂-C₄ alkenyl;

R²⁹ is independently selected at each occurrence from the group: R³⁰, H, C₁-C₆ alkyl, phenyl, benzyl, and trifluoromethyl;

R³⁰ is a bond to L_n;

or a pharmaceutically acceptable salt thereof.

56. (amended) A therapeutic radiopharmaceutical composition, comprising:

- (a) a therapeutic radiopharmaceutical comprising: a metal, a chelator capable of chelating the metal, a targeting moiety, and a linking group present between the targeting moiety and chelator;

wherein the targeting moiety is bound to the chelator, is an indazole nonpeptide and binds to a receptor that is upregulated during angiogenesis;

wherein the metal is a radioisotope selected from the group: ³³P, ¹²⁵I, ¹⁸⁶Re, ¹⁸⁸Re, ¹⁵³Sm, ¹⁶⁶Ho, ¹⁷⁷Lu, ¹⁴⁹Pm, ⁹⁰Y, ²¹²Bi, ¹⁰³Pd, ¹⁰⁹Pd, ¹⁵⁹Gd, ¹⁴⁰La, ¹⁹⁸Au, ¹⁹⁹Au, ¹⁶⁹Yb, ¹⁷⁵Yb, ¹⁶⁵Dy, ¹⁶⁶Dy, ⁶⁷Cu, ¹⁰⁵Rh, ¹¹¹Ag, and ¹⁹²Ir; and,

- (b) a parenterally acceptable carrier.